

Amendments to the Claims:

Please cancel claims 2 and 3.

1. (Currently Amended) A method for detecting mutation in an HBV-derived nucleic acid target sequence in a sample, said method comprising:
 - subjecting the sample to denaturing conditions to yield single stranded forms of said target sequence;
 - contacting the denatured sample with a set of first and second primers comprising at least two primers wherein at least one the first primer is capable of hybridizing hybridizes under high stringency conditions to a region encoding the N-terminus of the major hydrophilic loop of HBV surface antigen one strand of said target sequence and wherein at least one other and the second primer is capable of hybridizing hybridizes under high stringency conditions to another region downstream from the C-terminus of the major hydrophilic loop of HBV surface antigen a strand complementary to said first mentioned strand and wherein said primers are extendable from their 3' termini to form an extension product complementary to the strand to which each of said primers has hybridized and;
 - subjecting the sample to primer extension and amplification conditions to facilitate amplification to generate an amplified primer extension product comprising complementary extension products; and then
 - determining whether the amplified product comprises nucleic acid encoding major HBV surface antigen (SHBsAg) having a mutation at amino acid position 130, 131, 133 or 145, or having mutations at amino acid positions 130 and 145, 130 and 133, 131 and 145, or 133 and 145
2. (Canceled)
3. (Canceled)
4. (Currently Amended) A method according to Claim 1 ~~or 2 or 3~~, further comprising:
 - first subjecting the sample to reverse transcription conditions to yield single or double stranded cDNA molecules from HBV-derived mRNA.
5. (Currently Amended) A method according to Claim 1 wherein ~~one of said primers is labeled~~ the first primer is labeled with a reporter molecule capable of giving an identifiable signal

~~and the other of said primers is labeled~~ the second primer is labeled with a capturable moiety, ~~or the first primer is labeled with a capturable moiety and the second primer is labeled with a reporter molecule capable of giving an identifiable signal.~~

6. (Currently Amended) A method according to claim 5 wherein the primer labeled with a capturable moiety is immobilized to a solid support ~~for detecting an HBV-derived DNA target sequence in a sample, said method comprising introducing said sample to a reaction vessel having a primer immobilized to a solid support and a second primer in solution phase wherein both primers are capable of hybridizing to a complementary nucleotide sequence on complementary single strands of HBV-derived DNA in a region within, proximal or adjacent to a conserved region on the HBV genome and wherein the solution phase primer is labelled with a reporter molecule capable of giving an identifiable signal, subjecting the reaction vessel to conditions to facilitate amplification and then detecting the presence of the identifiable signal wherein the presence of said signal is indicative of the presence of HBV-derived DNA.~~

7. (Currently Amended) A method for detecting mutation in one or more ~~an~~ HBV-derived DNA target sequences in a sample from the same or different strains or variants of HBV, said method comprising:

contacting a the sample putatively comprising HBV-derived DNA in single stranded form with two or more a library of first primers immobilized individually or in an array to a solid support in a reaction vessel, wherein the reaction vessel further comprises solution phase a library of second primers existing in a solution phase and each having one of the first primers as a an amplification partner immobilized to the solid support wherein the immobilized; first primer is labeled with a capturable moiety; and its solution phase partner the second primer is labeled with a reporter molecule; are capable of amplifying under

subjecting the sample in the reaction vessel to amplifying conditions to generate a library of immobilized amplified products each encoding a region of HBV-derived DNA wherein the solution phase primer carries a reporter molecule capable of giving an identifiable signal such that the presence of a signal at a defined location on the solid support enables the identification of a particular HBV isolate or variant; and

determining whether each of the amplified products comprises nucleic acid encoding major HBV surface antigen (SHBsAg) having a mutation at amino acid position 130, 131, 133 or 145, or having mutations at amino acid positions 130 and 145, 130 and 133, 131 and 145, or 133 and 145.

8. (Withdrawn)
9. (Withdrawn)
10. (Currently Amended) A method according to Claim 1 wherein the first primer comprises SEQ ID NO: 1 and the second primer comprises SEQ ID NO: 2 ~~the primers are selected from <400>1 and <400>2 or primers having at least 70% similarity thereto or primers capable of hybridizing to <400>1 or <400>2 under low stringency conditions.~~
11. (Withdrawn)
12. (Withdrawn)
13. (New) A method according to Claim 5 wherein the capturable moiety is biotin and the reporter molecule is fluorescein or Orcein Red.
14. (New) A method according to Claim 1 wherein the mutation at position 130 is from glycine to aspartic acid.
15. (New) A method according to Claim 1 wherein the mutation at position 131 is from threonine to asparagine.
16. (New) A method according to Claim 1 wherein the mutation at position 133 is from methionine to threonine.
17. (New) A method according to Claim 1 wherein the mutation at position 145 is from glycine to arginine.
18. (New) A method according to Claim 1 wherein the mutations at positions 130 and 145 are from glycine to aspartic acid at position 130, and from glycine to arginine at position 145.
19. (New) A method according to Claim 1 wherein the mutations at positions 130 and 133 are from glycine to aspartic acid at position 130, and from methionine to threonine at position 133.

20. (New) A method according to Claim 1 wherein the mutations at positions 131 and 145 are from threonine to asparagine at position 131, and from glycine to arginine at position 145.
21. (New) A method according to Claim 1 wherein the mutations at positions 130 and 145 are from methionine to threonine at position 133, and from glycine to arginine at position 145.
22. (New) A method for evaluating whether a sample contains HBV that may have escaped immunological detection, said method comprising the steps of:
- i) contacting the sample with a set of first and second primers wherein the first primer hybridizes under high stringency conditions to a region encoding the N-terminus of the major hydrophilic loop of HBV surface antigen and the second primer hybridizes under high stringency conditions to another region downstream from the C-terminus of the major hydrophilic loop of HBV surface antigen;
 - ii) performing PCR on the mixture generated in step i) to generate an amplified primer extension product; and
 - iii) determining whether the amplified product comprises nucleic acid encoding major HBV surface antigen (SHBsAg) having a mutation at amino acid position 130, 131, 133 or 145, or having mutations at amino acid positions 130 and 145, 130 and 133, 131 and 145, or 133 and 145, identification of said mutation indicating that the sample contains HBV that may have escaped immunological detection.
23. (New) A method according to Claim 22 wherein the first primer comprises SEQ ID NO: 1 and the second primer comprises SEQ ID NO: 2.
24. (New) A method according to Claim 22 wherein the mutation at position 130 is from glycine to aspartic acid.
25. (New) A method according to Claim 22 wherein the mutation at position 131 is from threonine to asparagine.
26. (New) A method according to Claim 22 wherein the mutation at position 133 is from methionine to threonine.

27. (New) A method according to Claim 22 wherein the mutation at position 145 is from glycine to arginine.
28. (New) A method according to Claim 22 wherein the mutations at positions 130 and 145 are from glycine to aspartic acid at position 130, and from glycine to arginine at position 145.
29. (New) A method according to Claim 22 wherein the mutations at positions 130 and 133 are from glycine to aspartic acid at position 130, and from methionine to threonine at position 133.
30. (New) A method according to Claim 22 wherein the mutations at positions 131 and 145 are from threonine to asparagine at position 131, and from glycine to arginine at position 145.
31. (New) A method according to Claim 22 wherein the mutations at positions 130 and 145 are from methionine to threonine at position 133, and from glycine to arginine at position 145.
32. (New) A method for evaluating whether a sample contains HBV that may be resistant to anti-HBV drug treatment, said method comprising the steps of:
- i) contacting the sample with a set of first and second primers wherein the first primer hybridizes under high stringency conditions to a region encoding the N-terminus of the major hydrophilic loop of HBV surface antigen and the second primer hybridizes under high stringency conditions to another region downstream from the C-terminus of the major hydrophilic loop of HBV surface;
 - ii) performing PCR on the mixture generated in step i) to generate an amplified primer extension product; and
 - iii) determining whether the amplified product comprises nucleic acid encoding major HBV surface antigen (SHBsAg) having a mutation at amino acid position 130, 131, 133 or 145, or having mutations at amino acid positions 130 and 145, 130 and 133, 131 and 145, or 133 and 145, identification of said mutation indicating that the sample contains HBV that may be resistant to anti-HBV drug treatment.
- 33 (New) A method according to Claim 32 wherein the anti-HBV drug is lamivudine.

34. (New) A method according to Claim 32 wherein the first primer comprises SEQ ID NO: 1 and the second primer comprises SEQ ID NO: 2.
35. (New) A method according to Claim 32 wherein the mutation at position 130 is from glycine to aspartic acid.
36. (New) A method according to Claim 32 wherein the mutation at position 131 is from threonine to asparagine.
37. (New) A method according to Claim 32 wherein the mutation at position 133 is from methionine to threonine.
38. (New) A method according to Claim 32 wherein the mutation at position 145 is from glycine to arginine.
39. (New) A method according to Claim 32 wherein the mutations at positions 130 and 145 are from glycine to aspartic acid at position 130, and from glycine to arginine at position 145.
40. (New) A method according to Claim 32 wherein the mutations at positions 130 and 133 are from glycine to aspartic acid at position 130, and from methionine to threonine at position 133.
41. (New) A method according to Claim 32 wherein the mutations at positions 131 and 145 are from threonine to asparagine at position 131, and from glycine to arginine at position 145.
42. (New) A method according to Claim 32 wherein the mutations at positions 130 and 145 are from methionine to threonine at position 133, and from glycine to arginine at position 145.